



# Telephone consultation for myasthenia gravis care during the COVID-19 pandemic: Assessment of a novel virtual myasthenia gravis index

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## Abstract

**Introduction/Aims:** The aim of the study was to determine the association between the virtual Myasthenia Gravis Impairment Index (vMGII) with other patient-reported outcomes (PROs) of myasthenia gravis (MG) and its usefulness in telephone consultations with MG patients.

**Methods:** This was a retrospective case series in which vMGII score along with virtual Single Simple Question (vSSQ), virtual Patient-Acceptable Symptom State PASS (vPASS) response, and patient disease status based on Myasthenia Gravis Foundation of America postintervention status were collected during telephone consultation along with the MGII, SSQ, and PASS responses during the preceding in-person clinic visits.

**Results:** In 214 patients, the mean difference of vMGII between the vPASS “Yes” and “No” groups was  $-14.2 \pm 1.4$  (95% confidence interval,  $-16.9$  to  $-11.3$ ;  $P < .001$ ) with mean vMGII for vPASS “Yes” group being  $6.4 \pm 7.7$  and vPASS “No” being  $20.5 \pm 11.5$ . A vMGII of 11.5 or higher predicted vPASS “yes” response with a sensitivity of 78.7% and specificity of 81.4%. A strong negative correlation was found between the vMGII and vSSQ ( $r = -.667$ ;  $P < .001$ ). The mean vMGII was  $0.48 \pm 1.42$  for patients in remission, and  $9.31 \pm 10.93$  for improved,  $9.32 \pm 8.79$  for stable, and  $22.58 \pm 14.04$  for worsened groups ( $P < .001$ ). These associations were the same as those obtained during the preceding in-person clinic visit and the direction of change in MGII scores also indicated change in disease status.

**Discussion:** vMGII is an effective measure to assess an MG patient's disease status in telephone consultations and relates well with other PRO measures. The vMGII remains reliable for assessing MG disease status even with removal of the physical examination component.

**Abbreviations:** AChR, acetylcholine receptor; CSR, chronic stable remission; IVIg, intravenous immunoglobulin; MG, myasthenia gravis; MG-ADL, Myasthenia Gravis-Activities of Daily Living; MGFA PIS, Myasthenia Gravis Foundation of America postintervention status; MGII, Myasthenia Gravis Impairment Index; MuSK, muscle-specific tyrosine kinase; PASS, Patient-Acceptable Symptom State; PR, pharmacological remission; PRO, patient-reported outcomes; QMGs, Quantitative Myasthenia Gravis Score; ROC, receiver operating characteristic; SClg, subcutaneous immunoglobulin; SSQ, Simple Single Question; vMGII, virtual Myasthenia Gravis Impairment Index; vPASS, virtual Patient Acceptable Symptom State; vSSQ, virtual Simple Single Question.

## KEYWORDS

myasthenia gravis, Myasthenia Gravis Impairment Index, patient-reported outcomes, telephone consultation

## 1 | INTRODUCTION

Unprecedented restrictions enforced by the COVID-19 pandemic have induced adaptations in health-care delivery systems, which have led to expansion of virtual care. Telephone consultations are well-known modalities in virtual care and are promising platforms through which continued medical care can be provided, especially to patients with chronic neurological conditions.<sup>1,2</sup> However, without the physical examination, physicians have to base their decision-making exclusively on patient-reported symptoms. In this regard, myasthenia gravis (MG) poses special challenges for virtual management by its fluctuating course and broad spectrum of symptoms. Measures that capture the disease status as comprehensively as possible are thus highly desirable for accurate assessment, and this can prove to be vital in making important treatment decisions. Among the various validated measures for assessing MG, the Myasthenia Gravis Impairment Index (MGII) has the advantage of composite scoring based on a patient self-reported multidomain questionnaire as well as physician-documented clinical measures.<sup>3,4</sup> An adapted version of the MGII, the virtual MGII (vMGII), was used to create a composite score based on patient responses obtained during telephone consultation, foregoing the physical examination item scores. The questionnaire component of the MGII has shown reliability and correlation with other relevant measures and has been used in a previous survey study of patients with MG.<sup>3,5</sup> Other easy-to-apply patient-reported outcomes (PROs), such as Patient-Acceptable Symptom State (PASS) response and Single Simple Question (SSQ) response, may also be valuable virtual tools in this respect; they have been examined previously and are being utilized in MG assessment.<sup>5-7</sup> The objective of the current study was to evaluate the association of vMGII with other established patient outcome measures and thus explore its usefulness in identifying MG disease status during telephone consultations.

## 2 | METHODS

We retrospectively collected data from consecutive patients who were followed-up through telephone consultation from the Prosserman Family Neuromuscular Clinic of the Toronto General Hospital from April 1, 2020 until August 15, 2020. Only patients older than 18 years of age and who had been seen at least once previously for an in-person clinic visit with a definite diagnosis of MG, defined by appropriate clinical history with single-fiber electromyography showing increased jitter, with or without seropositivity, were included.

During routine, continued, in-person MG clinic visits, we obtain MGII, SSQ, and PASS information, as well as patient history. Physical examination is performed, which includes Medical Research Council

scoring of muscle strength and forced vital capacity using a hand-held spirometer. Both PASS and SSQ are PROs and have been validated with the PASS “Yes” response, with higher SSQ percentages signifying better patient status.<sup>6,7</sup> MGII has 22 patient-reported and 6 physician-assessed items with a final composite score of 84, with higher score signifying greater disability.<sup>3</sup>

Since the beginning of the restrictions enforced by the COVID pandemic, we were engaged in telephone consultations for follow-up of patients with MG. During each teleconsultation history regarding the patient's current symptoms and disabilities, medication doses and side-effects and other comorbid medical issues were obtained along with PASS (vPASS) and SSQ (vSSQ) responses. The vMGII was generated by reading out to the patient all of the patient-reported sections of the MGII, recording patient responses, and tallying the scores of these 22 items, scored from 0 to 3 or 4, with a total score of 68. Disease status was graded as worse, stable, improved, or in remission (pharmacological remission [PR] and chronic stable remission [CSR]) based on the Myasthenia Gravis Foundation of America post-intervention classification status (MGFA PIS) compared with the previous visit. Through chart review we also collected age and gender data; duration of MG; clinical phenotype; antibody, thymectomy status along with thymic pathology; and the MGII, PASS, and SSQ responses during the previous in-person clinic visit. The current treatment data were collected, classified as none or only symptomatic treatment with pyridostigmine, along with number of immunosuppressants. All patients were interviewed by clinical fellows working in the neuromuscular clinic who were experienced neurologists, all of whom were well-versed in use of the MG assessment scales. Each case was then reviewed by the attending staff. The study was approved by the research ethics board of the University Health Network.

### 2.1 | Statistical analysis

SPSS version 20 software (IBM Corp, Armonk, New York) was used for data analysis. Data used to describe the demographic and clinical variables are presented as mean and standard deviation or as number and percent, as appropriate. Comparison of the vMGII with vPASS was done using independent *t* tests, whereas that with vSSQ was done with Pearson correlations. A receiver operating characteristic (ROC) curve was drawn between vMGII and vPASS to determine the vMGII cut-off that would predict the PASS “yes” response. We expected to find similar thresholds to those of previous studies. Analysis of variance was used to compare the means of vMGII between the MG diseases status based on MGFA PIS during the telephone consultation. As an internal control, an association and correlation was also drawn between the MGII and the corresponding PASS and

SSQ during the previous inpatient visit. Last, the difference in scores between the vMGII and the previous MGII obtained during the clinical visit (delta MGII) was obtained, and its association with MG disease status (MGFA PIS) was determined during telephone consultation.  $P < .05$  was considered statistically significant. When possible, missing data were imputed according to the instructions of each outcome measure.

**TABLE 1** Demographic variables

Variable	Values <sup>a</sup>
Number of patients	214
Age, years <sup>b</sup>	61.5 ± 15.8
Males/females	81 (37.9%) / 133 (62.1%)
Duration of MG, years	10.0 ± 8.2
Generalized MG	180 (84.1%)
Ocular MG	34 (15.9%)
Antibody-positive	120 (56.1%)
AChR	113 (52.8%)
MUSK	7 (3.3%)
Antibody-negative <sup>b</sup>	87 (40.7%)
Thymectomy	115 (53.7%)
Thymic pathology	
Thymoma	49 (42.6%)
Thymic hyperplasia	21 (18.3%)
Involutional/remission	25 (21.7%)
Duration since thymectomy, years (n = 115)	11.9 ± 9.1
Comorbidities <sup>c</sup>	
None	138 (64.5%)
Musculoskeletal disorders	16 (7.5%)
End-organ damage <sup>d</sup>	16 (7.5%)
Depression	9 (4.2%)
Cancer or history of cancer	11 (5.9%)
Multiple systemic disorders	19 (8.9%)
Skin disease	5 (2.3%)
Treatment	
No treatment	13 (6.1%)
Only pyridostigmine	16 (7.5%)
IVIg/SCIg/PLEx	34 (15.8%)
1 immunosuppressant	79 (36.9%)
2 immunosuppressants	66 (30.8%)
3 immunosuppressants	2 (0.9%)

Abbreviations: AChR, acetylcholine receptor; IVIg, intravenous immunoglobulin; MG, myasthenia gravis; MuSK, muscle-specific tyrosine kinase; PLEx, plasma exchange; SCIg, subcutaneous immunoglobulin.

<sup>a</sup>Values are presented as number, mean ± standard deviation, or number (%).

<sup>b</sup>Data not available for 7 patients.

<sup>c</sup>Does not include diabetes, hypertension, or dyslipidemia without any complications/end-organ damage.

<sup>d</sup>End-organ damage refers to any of symptomatic heart disease, lung disease, kidney disease, or other neurological diseases.

### 3 | RESULTS

We identified 214 patients with MG who had telephone consultations during the study period and who satisfied the selection criteria. The mean age of the patients was 61.5 ± 15.8 years. The majority (n = 133, 62.1%) were female. Detailed demographic and clinical parameters are summarized in Table 1.

**TABLE 2** Comparison of vMGII and demographic and clinical variables

Variable	Virtual MGII score (mean ± SD)	P value
Males	6.4 ± 7.5	<.001 <sup>a</sup>
Females	11.3 ± 11.5	
Generalized MG	10.3 ± 10.7	.002 <sup>a</sup>
Ocular MG	5.1 ± 7.2	
Antibody-positive		
AChR	7.1 ± 8.1	.001 <sup>a</sup>
MuSK	14 ± 14.4	
Antibody-negative <sup>b</sup>	12.5 ± 12	
Thymectomy		.286
Yes	9.3 ± 10.5	
No	9.7 ± 10.4	
Thymic pathology		.750
Thymoma	9.4 ± 10.0	
Thymic hyperplasia	7.7 ± 10.0	
Involutional/remission	10.7 ± 9.5	
Comorbidities		
None	8.2 ± 8.9	<.001 <sup>c</sup>
Musculoskeletal disorders	11.4 ± 14.9	
End-organ damage	6.6 ± 5.9	
Depression	20.9 ± 9.9	
Cancer or history of cancer	6.9 ± 7.1	
Multiple systemic disorders <sup>d</sup>	14.8 ± 16.4	
Skin disease	12.6 ± 3.8	
Treatment		.030 <sup>c</sup>
No treatment	10.9 ± 14.3	
Only pyridostigmine	12.4 ± 12.8	
IVIg/SCIg/PLEx	13.3 ± 12.5	
1 immunosuppressant	6.9 ± 8.1	
2 immunosuppressants	9.1 ± 9.6	
3 immunosuppressants	17.0 ± 16.9	

Abbreviations: AChR, acetylcholine receptor; IVIg, intravenous immunoglobulin; MG, myasthenia gravis; MGII, Myasthenia Gravis Impairment Index; MuSK, muscle-specific tyrosine kinase; PLEx, plasma exchange; SCIg, subcutaneous immunoglobulin; SCIg, subcutaneous immunoglobulin; SD, standard deviation.

<sup>a</sup>Independent sample *t* test.

<sup>b</sup>Data from 87 patients (7 not available).

<sup>c</sup>Analysis of variance.

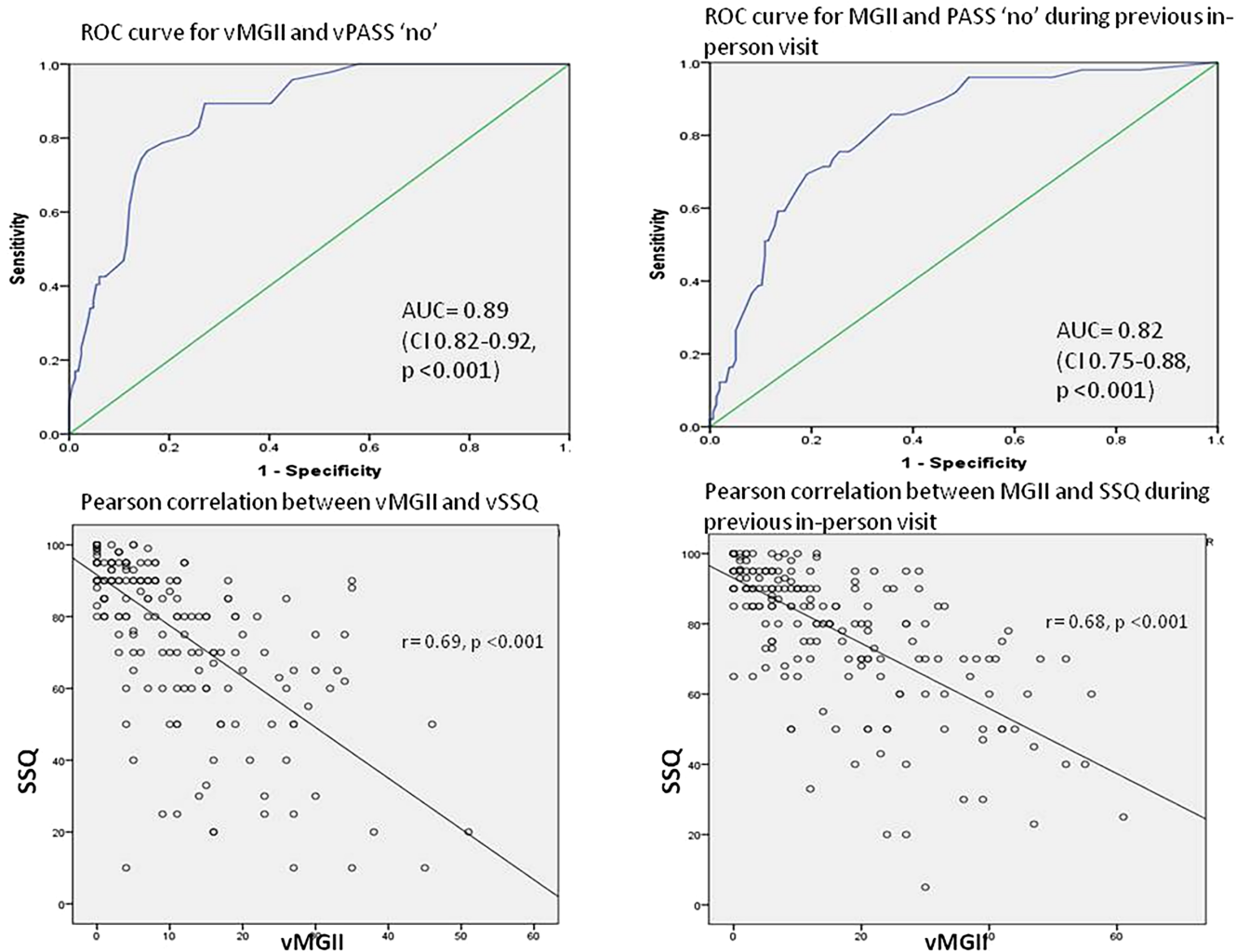
<sup>d</sup>Multiple systemic disorders—when the patient had 2 or more systemic conditions (other than MG) that required continued medical treatment.

From data obtained during the telephone consultations we found that 167 (78%) patients responded affirmatively to vPASS (vPASS “yes”), and the mean vSSQ was  $78.3 \pm 22.2\%$ . Twenty-five (11.7%) patients were in remission (PR or CSR), 29 (13.6%) improved, 141 (65.9%) were stable, and 19 (8.9%) worsened. There were significant differences in mean vMGII with regard to gender, serology status, comorbidities, and treatment (Table 2). Post hoc analysis showed a significant difference in vMGII scores only for depression among comorbidities and for patients on three immunosuppressants and intravenous immunoglobulin/plasma exchange treatment.

The vMGII with vPASS, vSSQ, and patient disease status based on MGFA PIS were compared. The mean vMGII for the vPASS “yes” group was  $6.4 \pm 7.7$  and for the vPASS “no” it was  $20.5 \pm 11.5$  (mean difference,  $-14.2 \pm 1.4$ ; 95% confidence interval,  $-16.9$  to  $-11.3$ ;  $P < .001$ ). The ROC curve drawn between vMGII and vPASS showed that the area under the curve (AUC) was high (Figure 1). A vMGII of 11.5 or less predicted vPASS “yes” response with a sensitivity of 78.7% and specificity of 81.4%, positive predictive value of 93.9%,

and negative predictive value of 51.7%. A strong negative correlation was found between vMGII and vSSQ. An SSQ of 68.5% or more was able to detect PASS “yes” response with a sensitivity of 90.4% and specificity of 78.3%, positive predictive value of 80.3%, and negative predictive value of 69.8%. The ROC AUC between vMGII and vPASS and the Pearson correlation coefficient between vMGII and vSSQ were comparable with corresponding measures for MGII, PASS, and SSQ during the previous clinic visit (Figure 1).

The mean vMGII was significantly different across the remission, improved, stable, and worsened groups (Table 3). Post hoc groupwise analysis revealed significant differences in mean vMGII scores between all groups, except between improved and stable patients. The difference in scores between the PR section of the MGII from the previous visit and the current vMGII, that is, delta MGII, showed an association with MGFA PIS. Those patients with improved (mean delta MGII,  $7.7 \pm 11.0$ ), remission (mean delta MGII,  $3.6 \pm 7.8$ ), or stable (mean delta MGII,  $3.2 \pm 7.7$ ) status showed a positive change or decrease in vMGII, whereas an increase in score was associated with



**FIGURE 1** Comparisons between ROC curves and Pearson correlation coefficients for Myasthenia Gravis Impairment Index (virtual MGII and MGII) with other patient-reported outcomes. Abbreviations: AUC, area under curve; CI, confidence interval;  $r$ , correlation coefficient; ROC, receiver operating characteristic [Color figure can be viewed at [wileyonlinelibrary.com](http://wileyonlinelibrary.com)]

**TABLE 3** Comparison of mean vMGII scores across MGFA PIS

MGFA PIS	vMGII (mean ± SD)	95% CI for mean	P value <sup>a</sup>
Remission	0.48 ± 1.42	0.11-1.07	<.001
Improved	9.31 ± 10.93	5.15-13.47	
Stable	9.32 ± 8.79	7.86-10.78	
Worsened	22.58 ± 14.04	15.64-29.52	

Abbreviations: CI, confidence interval; MGFA PIS, Myasthenia Gravis Foundation of America postintervention status; SD, standard deviation; vMGII, virtual Myasthenia Gravis Impairment Index.

<sup>a</sup>Analysis of variance.

worsened patient status (mean delta MGII, 11 ± 9.2) ( $P = .016$ ). None of the patients in our cohort had MG exacerbations or crisis requiring emergency care referral.

## 4 | DISCUSSION

In this study of a large cohort of patients with MG who had telephone consultations during the COVID-19 era, we found that vMGII scores had an excellent correlation with the other PROs, namely vPASS and vSSQ. In addition, vMGII reflected patient disease status, with lower scores pointing to better outcome. The vMGII performed equally well compared with the MGII obtained during the previous in-person clinic visit, and a direction of change in scores between the in-person and virtual visit also predicted the change in disease status.

The advantage of telephone consultation as a virtual care platform is that it is the most accessible and least technically demanding to arrange, especially from a patient's perspective.<sup>8</sup> However, the lack of means for physical assessment is the major drawback and raises challenges not only for a first-time consultation, but also for patients followed for chronic neurological conditions.<sup>9</sup> Some of these challenges can be circumvented by utilizing a patient-reported rating score in assessing disease severity and also for comparisons across serial virtual assessments. In fact, MG rating scales, such as the adapted versions of Quantitative Myasthenia Gravis Score (QMGS) and the Myasthenia Gravis-Activities of Daily Living (MG-ADL) scale have been suggested as potential virtual tools, but, to the authors' knowledge, have not been tested prospectively in a significant number of patients with MG.<sup>10,11</sup> MGII has the advantage over MG-ADL in having less of a floor effect, and has advantages over the QMGS in that the MGII is simpler, less time-consuming, and is centered around the patient's symptoms.<sup>3,12</sup> Its strong correlation with other PROs, such as PASS and SSQ, has been also established.<sup>5-7</sup>

It is uncertain whether the responses obtained via a telephone interview differ from those obtained through a face-to-face interview.<sup>13</sup> For the vMGII, the mode of questionnaire administration may affect the patient response.<sup>14</sup> For in-person consultations, during which the questionnaires are answered without interaction with the health-care provider, the patients have more time to contemplate and reflect or get a bystander's opinion to aid in their responses.<sup>15</sup> It may be that in-person responses have better reliability than telephone-

administered surveys in certain research settings.<sup>16</sup> Most importantly, it was uncertain the extent to which the absence of the physical examination subsection, which contributes a maximum of 16 points on the MGII, could influence the performance of the vMGII. Our findings allay these concerns by showing vMGII to be equally effective in determining MG severity. Despite the lack of a physical exam component, the vMGII showed excellent correlations with PASS, SSQ, and disease status of the patient. In many other aspects, the vMGII had similar properties to the MGII. The vMGII scores were lowest for patients who were in remission and highest among those with worsening status, which is also consistent with the properties of the MGII. Our results show that the lack of a physical examination section from the MGII did not impact the ability of the vMGII to reflect the patient's assessment and satisfaction, or lack thereof, with respect to their disease state. This is likely because the physical examination contributes less to the MGII than the patient-reported section because the MGII is weighted in favor of patient-reported symptoms over the most recent 2 weeks and, in MG, this score may not always reflect the neurologist's findings during the clinic visit.

The internal comparisons for the associations between vMGII, vPASS, and vSSQ and for MGII with the corresponding PASS and SSQ during the previous clinic visit showed excellent results. Thus, vMGII correlated with vPASS and vSSQ as well as the in-person MGII. This is further confirmed by the observation that not only absolute vMGII score, but also the change in MGII score, was associated with disease status. A negative change in vMGII score compared with the previous patient-reported section of the MGII score also correlated with MG worsening, whereas a positive change showed a better outcome. The degree of change in the MGII among in the various groups was also comparable with that observed in our earlier study.<sup>5</sup> The broader practical implication is that utilizing a more complex and time-consuming audio-video interface to perform clinical examination may not be cost-effective or contribute greatly to the monitoring of MG patients. Moreover, only a small fraction (2.8%) of our cohort required an in-person clinic visit due to the inability to reach a conclusion based on the telephone consultation. Thus, a telephone consultation when incorporating relevant clinical scores is sufficient for monitoring most patients with MG.

Although previous studies showed that PROs obtained via phone interviews were not inferior to self-survey by patients in the clinic, the method of administering the questionnaire likely impacts patient responses.<sup>14,17,18</sup> Although in most cases the vMGII was collected at the beginning of the interview, this procedure was not followed in all telephone consultations performed in our study, and interviewer bias is inherent in this mode of response collection. Both of these are limitations of the study. In a prospective study, a blinded rater may be used, but the current methodology is pragmatic and best suited to examining the utility of the vMGII in the real-world setting. In addition, in this cohort all patients were familiar with the MGII from their routine clinic visits, which probably made phone assessment easier. Another method that may make telephone assessment more efficient would be to send the online questionnaire to the patient for completion before the telephone interview, and such an approach may be

investigated in the future. A drawback intrinsic to most PRO measures is the impact of psychological health and other medical comorbidities on patient responses.<sup>19,20</sup> In the current study, higher vMGII scores were observed for patients with comorbidities, most significantly among those with depression. Similar discrepancies have been noted during in-person clinical visits, even with full MGII and routine clinical assessment. As such, this limitation is not unique to the virtual world, and in most situations a relevant history reveals the true cause of the apparent worsening in disease status. Last, our study was a single-center investigation and had a relatively low percentage of patients with seropositivity,<sup>21,22</sup> which cautions against the generalizability of our findings. Further multicenter, cross-cultural studies are required.

In conclusion, in this study we have shown that the vMGII is a valuable and simple way to provide telephone care to MG patients and that it associates well with other PRO measures and disease status. The lack of a physical examination did not prevent the vMGII from providing an MG disease assessment that was comparable to that with a full MGII, and therefore a visual media interface may not be more informative. Future prospective studies will be needed to establish vMGII as a standard of care in telephone consultations for MG.

#### CONFLICT OF INTEREST

The authors declare no potential conflicts of interest.

#### ETHICAL PUBLICATION STATEMENT

We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

#### DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request

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